AD_____

Award Number: W81XWH-12-1-0160

TITLE: Investigating Genomic Mechanisms of Treatment Resistance in Castration Resistant Prostate Cancer

PRINCIPAL INVESTIGATOR: Terence W. Friedlander, M.D.

CONTRACTING ORGANIZATION: University of California, San Francisco
San Francisco, CA 94143

REPORT DATE: May 2013

TYPE OF REPORT: Annual Summary

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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Investigating Genomic Mechanisms of Treatment Resistance in Castration Resistant Prostate Cancer

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5b. GRANT NUMBER
W81XWH-12-1-0160

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Terence W. Friedlander, M.D.

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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

University of California, San Francisco
San Francisco, CA 94143

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT
Purpose and Scope: The purpose of this work is to better understand the mechanisms of resistance to androgen biosynthesis inhibitors in men with castration resistant prostate cancer, and to investigate clinical methods of overcoming resistance.

Key Accomplishments and Findings to date:
• CTCs collected in 12 men with abiraterone-naïve mCRPC. These cells are in the process of enumeration, immunocytochemical analysis for expression of prostate-specific cell surface markers, and DNA isolation. CTCs thus far are detectable in >90% of men using the Vitatex VitaCaP assay. CTCs expressing a mesenchymal phenotype are detectable as well as those bearing markers of stemness including CD44. CTCs from this assay are amenable to flow cytometry both for enumeration and for sorting of different CTC subpopulations. Further genomic analysis of CTC subpopulations to be detailed in subsequent updates. • Phase II protocol for Dose-Increased Abiraterone Acetate in Men with mCRPC (PI: Friedlander) written, IRB approved, and accruring patients at by UCSF and Oregon Health Sciences University.

• Phase II protocol of Abiraterone Acetate plus ARN-5
09 in men with mCRPC (PI: Friedlander) completed, approved by UCSF site-review committee, and in further development at UCSF and at Dana Farber Cancer Institute.

• Integration of both clinical trials with recently awarded Stand Up 2 Cancer "West Coast Dream Team" castration-resistant prostate cancer biopsy protocol, allowing for even more comprehensive molecular and genomic analysis of mechanisms of abiraterone/ABI resistance.

15. SUBJECT TERMS
Prostate cancer, castration-resistant prostate cancer, abiraterone, androgens, circulating tumor cells, treatment resistance

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
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INTRODUCTION

Although androgen biosynthesis inhibitors (ABIs) including ketoconazole and abiraterone improve clinical outcomes and prolong survival in men with castration resistant prostate cancer (CRPC), none are curative, and all patients eventually develop resistance followed by disease progression and death. Resistance is hypothesized to result from either increased systemic or tumor androgen production, mutations in the androgen receptor (AR) signaling pathway leading to ligand-independent AR activity, or through AR-independent pathways. The work being carried out under this grant aims to better understand how this therapeutic resistance develops through genomic analysis (gene copy number and gene methylation status) of tumor biopsies and circulating tumor cells (CTCs) taken from men with CRPC. Further, the work here explores whether clinically targeting proposed mechanisms of resistance can improve outcomes in these patients.

BODY

Statement of Work Aim A: Determine whether resistance to androgen biosynthesis inhibitors (ABIs) is mediated by genomic upregulation of androgen synthesis or by autonomous AR function.

Thus far much of the work for this Aim has been for Task 1 as follows: a protocol for the collection of metastatic biopsies and circulating tumor cells (CTCs) has been developed, reviewed by both the scientific and IRB committees at UCSF and approved. A laboratory specific protocol (CC125511, see attachments) detailing the genomic tests to be performed on CTCs was developed and approved by both UCSF and the DoD IRB. The CTCs are currently being collected as part of a clinical trial of increased-dose abiraterone (CC12551, see attachment) detailed below in Aim B of this summary.

In late 2012 our group at UCSF was extremely fortunately to be awarded a grant to collect and analyze metastatic CRPC biopsies to better understand treatment resistance, as part of the Stand Up 2 Cancer "West Coast Dream Team" study, and thus the collection and analysis of metastatic biopsies for this DoD grant has been fully integrated with the Dream Team study. In this protocol metastatic biopsies from men with CRPC are collected and the genomic tests described in this grant are set to be performed by our lab. At the same time other comprehensive genomic tests (RNAseq, microRNA analysis, targeted gene sequencing) will be performed by other collaborators in the West Coast Dream Team consortium, allowing for an even greater in-depth analysis of CRPC tumors.

For both the CTC work and for the biopsy protocol clinical and lab staff at UCSF have been trained in how to collect and process samples, and a protected database has been established to track and annotate specimens. Thus far we have collected blood from 12 men with abiraterone-naïve CRPC. CTCs are detectable in >90% of these samples using the Vitatex VitaCaP assay. Thee CTCs express epithelial markers including PSMA, and DNA isolation from these cells is feasible. CTCs expressing a mesenchymal phenotype are detectable as well as those bearing markers of stemness including CD44 (unpublished results). CTCs from this assay are amenable to flow cytometry both for enumeration and for sorting of different CTC subpopulations including those expressing epithelial markers, mesenchymal markers, and markers of stemness. Biopsies thus far have been

collected from 10 men with abiraterone-naïve disease are currently being processed (pathology review, DNA, RNA isolation) by the Dream Team sites. Copy number and methylation analysis of androgen synthesis genes taken from CTCs and biopsies from men prior to abiraterone and after abiraterone resistance has developed will occur in batch once sufficient samples have been isolated.

Statement of Work Aim B: Determine whether resistance to ABIs s can be overcome by increased inhibition of androgen synthesis.

As discussed above, a clinical protocol for increased-dose abiraterone has been written, approved by both the peer-review/scientific committees at UCSF and at Oregon Health Science University (OHSU) and their respective IRBs, and the clinical trial opened and began accruing patients at each site in March 2013. OHSU was chosen as it is part of the DoD Prostate Cancer Clinical Trials Consortium as well as a collaborator in the Dream Team biopsy study.

The clinical trial of dose-increased abiraterone is registered with clinicaltrials.gov with the number NCT01637402. Accrual has been brisk, with approximately 20 men consented and/or on-study to date. Clinical research associates have been trained in study procedures at both sites, and we are using the UCSF OnCore database to collect and track patient information/data. Weekly review of patient accrual, compliance with study procedures, and safety review has begun. All patients to date have experienced PSA declines to standard-dose (1000mg daily) abiraterone, and none yet have experienced PSA or clinical progression warranting an elevated dose (1000mg twice daily). Blood is currently being collected for serum hormone levels, SNPs in androgen synthesis genes, and CTCs as described above. Optional metastatic biopsies are being offered to all participants, and approximately 50% of study participants have undergone biopsy prior to starting abiraterone therapy.

Statement of Work Aim C: Determine whether resistance to ABIs can be overcome by AR-targeted therapy.

A Phase I study of the combination of abiraterone acetate plus ARN-509 (a novel AR antagonist) is currently open at both UCSF and at Dana Farber Cancer Institute, a collaborator in the DoD Clinical Trials Consortium. One patient has thus far been accrued, and ARN-509 dose escalation will proceed once sufficient patients have been enrolled. At UCSF I have written a clinical protocol for a Phase II study of the combination of abiraterone acetate plus ARN-509. This has been reviewed by the UCSF Genitourinary Oncology Site Committee. The protocol in currently in revision and will be submitted to the UCSF Peer Review scientific committee for evaluation.

KEY RESEARCH ACCOMPLISHMENTS

- CTCs collected in 12 men with abiraterone-naïve mCRPC. These cells are in the process of enumeration, immunocytochemical analysis for expression of prostate-

specific cell surface markers, and DNA isolation. CTCs thus far are detectable in >90% of men using the Vitatex VitaCaP assay. CTCs expressing a mesenchymal phenotype are detectable as well as those bearing markers of stemness including CD44. CTCs from this assay are amenable to flow cytometry both for enumeration and for sorting of different CTC subpopulations. Further genomic analysis of CTC subpopulations to be detailed in subsequent updates.

- Phase II protocol for Dose-Increased Abiraterone Acetate in Men with mCRPC (CC12551, PI: Friedlander) written, IRB approved, and accruing patients at by UCSF and Oregon Health Sciences University (as part of the DoD Prostate Cancer Clinical Trials Consortium).

- Phase II protocol of Abiraterone Acetate plus ARN-509 in men with mCRPC (PI: Friedlander) completed, approved by UCSF site-review committee, and in further development at UCSF and at Dana Farber Cancer Institute.

- Laboratory protocol for copy number analysis of CTCs and metastatic biopsies (CC125511, PI: Friedlander) completed and approved by the IRBs at UCSF and the DoD.

- Integration of both clinical trials with recently awarded Stand Up 2 Cancer "West Coast Dream Team" CRPC biopsy protocol, allowing for even more comprehensive molecular and genomic analysis of mechanisms of abiraterone/ABI resistance.

REPORTABLE OUTCOMES

Thus far this work is in the beginning stages. Two clinical protocols and a laboratory protocol for the work have been developed or are under development and are either IRB approved or are in review by scientific committees. Thus far no abstract detailing this work has been submitted or presented, however a manuscript summarizing our lab experience with CTCs collected previously from 23 men with prostate cancer and analyzed on the Vitatex platform is currently being submitted for review and publication. In terms of other awards or grant funding, I received a 2012 Prostate Cancer Foundation Young Investigator Award to fund lab work in excess of that covered by the Physician Research Training Award yearly stipend, and a travel grant in 2012 to attend the Advances in Circulating Tumor Cells conference in Athens, Greece.

CONCLUSION

Significant progress has been made in terms of achieving goals set forth in the statement of work for this project, with activation of both the lab and clinical components proposed in the grant. Protocols allowing for collection and analysis of CTCs and CRPC biopsies have been completed and are accruing patients/samples, and a clinical trial of dose-increased abiraterone acetate has been IRB approved and opened at UCSF and OHSU. Collecting CTCs and biopsies from metastatic CRPC patients is feasible and an infrastructure for doing so has been developed at UCSF. Integration of the aims of this work with the Stand Up 2 Cancer West Coast "Dream Team" metastatic biopsy protocol has been achieved and is expected to allow for an even greater in-depth analysis of the

genomic mechanisms leading to androgen biosynthesis inhibitor resistance in men with metastatic CRPC.

REFERENCES
None

APPENDIX/SUPPORTING DATA
1. UCSF Cancer Center (clinical) protocol 12551: A Phase II Study of Increased-Dose Abiraterone Acetate in Patients with Castration Resistant Prostate Cancer (CRPC). Notice of IRB approval.

2. UCSF Cancer Center (lab) protocol 125511: Determination of Gene Copy Changes associated with Resistance to Androgen Biosynthesis Inhibitors in Men with Metastatic Castration Resistant Prostate Cancer. Notice of IRB approval.

3. Curriculum Vitae

University of California
San Francisco

Human Research Protection Program
Committee on Human Research

Notification of Expedited Review Approval

Principal Investigator
Terence W Friedlander

Co-Principal Investigator

Type of Submission: Modification Form
Study Title: CC#12551: A Phase II Study of Increased-Dose Abiraterone Acetate in Patients with Castration Resistant Prostate Cancer (CRPC)

IRB #: 12-08740
Reference #: 057068

Committee of Record: Mount Zion Panel

Study Risk Assignment: Greater than minimal

Approval Date: 11/6/2012 **Expiration Date:** 06/11/2013

Regulatory Determinations Pertaining to this Approval (if applicable):

IRB Comments (if applicable):

All changes to a study must receive CHR approval before they are implemented. Follow the modification request instructions. The only exception to the requirement for prior CHR review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103.b.4, 21 CFR 56.108.a). In such cases, report the actions taken by following these instructions.

Expiration Notice: The iMedRIS system will generate an email notification eight weeks prior to the expiration of this study's approval. However, it is your responsibility to ensure that an application for continuing review approval has been submitted by the required time. In addition, you are required to submit a study closeout report at the completion of the project.

Approved Documents: To obtain a list of documents that were approved with this submission, follow these steps: Go to My Studies and open the study – Click on Submissions History – Go to Completed Submissions – Locate this submission and click on the Details button to view a list of submitted documents and their outcomes.

For a list of all currently approved documents, follow these steps: Go to My Studies and open the study – Click on Informed Consent to obtain a list of approved consent documents and Other Study Documents for a list of other approved documents.

San Francisco Veterans Affairs Medical Center (SFVAMC): If the SFVAMC is engaged in this research, you must secure approval of the VA Research & Development Committee in addition to CHR approval and follow all applicable VA and other federal requirements. The CHR website has more information.

UCSF
University of California
San Francisco

Human Research Protection Program
Committee on Human Research

Notification of Expedited Review Approval

Principal Investigator
Terence W Friedlander

Type of Submission: Initial Review Submission Packet

Study Title: CC#125511: Determination of Gene Copy Changes associated with Resistance to Androgen Biosynthesis Inhibitors in Men with Metastatic Castration Resistant Prostate Cancer

IRB #: 12-08760

Reference #: 042284

Committee of Record: Mount Zion Panel

Study Risk Assignment: Minimal

Approval Date: 07/20/2012 **Expiration Date:** 07/19/2013

Regulatory Determinations Pertaining to this Approval (if applicable):

A waiver or alteration of informed consent is acceptable because, as detailed in the application: (1) the research involves no more than minimal risk to the subjects; (2) the waiver or alteration will not adversely affect the rights and welfare of the subjects; (3) the research could not practicably be carried out without the waiver or alteration; and (4) whenever appropriate, the subjects will be provided with additional pertinent information after participation.
The waiver or alteration of informed consent applies to all subjects.

The requirement for individual HIPAA authorization is waived for all subjects. The use or disclosure of the requested information does not adversely affect the rights and welfare of the individuals and involves no more than a minimal risk to their privacy based on, at least, the presence of the following elements:
(1) an adequate plan to protect the identifiers from improper use and disclosure; (2) an adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or if such retention is otherwise required by law;
(3) adequate written assurances that the requested information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the requested information would be permitted by the Privacy Rule;
(4) the research could not practicably be conducted without the waiver; and (5) the research could not practicably be conducted without access to and use of the requested information.

IRB Comments (if applicable):

All changes to a study must receive CHR approval before they are implemented. Follow the modification request instructions. The only exception to the requirement for prior CHR review and approval is when the changes are necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103.b.4, 21 CFR 56.108.a). In such cases, report the actions taken by following these instructions.

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University of California, San Francisco

CURRICULUM VITAE

Name: Terence W. Friedlander, MD

Position: HS Assistant Clinical Professor, Step 1
Medicine
School of Medicine

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University of California, San Francisco
San Francisco, CA 94143

Voice: 415 514-8481
Fax: 415 353-7093
email: terence.friedlander@ucsf.edu

EDUCATION

1995 - 1999	Brown University, Providence RI	BA	Biology
1999 - 2003	New York University Medical School	MD	Medicine
2003 - 2004	University of California, San Francisco	Internal Medicine Internship	Medicine
2004 - 2006	University of California, San Francisco	Internal Medicine Residency	Medicine
2006 - 2007	Utrecht University, Netherlands	MA	Medical Ethics
2007 - 2010	University of California, San Francisco	Fellowship	Hematology/Oncology
2009 - 2010	University of California, San Francisco	Chief Fellow	Hematology/Oncology
2010 - 2011	University of California, San Francisco	Fellowship	Urologic Oncology

LICENSES, CERTIFICATION

2004	Medical Licensure, California (Licence number A88888)
2006	American Board of Internal Medicine, Internal Medicine Certification
2010	American Board of Internal Medicine, Medical Oncology Certification

PRINCIPAL POSITIONS HELD

2011 -	University of California, San Francisco	Assistant Clinical Professor of Medicine	Medicine

HONORS AND AWARDS

2000	Herman Goldman Scholarship	NYU Medical School
2003	Spiegel Award for Academic Excellence	NYU Medical School
2003	Alpha Omega Alpha	National Medical Honors Society
2003	Medical Degree with Honors	NYU Medical School
2006	Fulbright Scholarship in Medical Ethics	Netherlands-America Foundation
2010	Young Investigator Award	American Society of Clinical Oncology
2012	Young Investigator Award	Prostate Cancer Foundation
2012	Physician Research Training Award	United States Department of Defense
2012	Travel Award	Advances in Circulating Tumor Cells Conference Foundation

KEYWORDS/AREAS OF INTEREST

Prostate Cancer, Bladder Cancer, genomics, microarrays, pharmacogenetics, circulating tumor cells, androgen biosynthesis inhibitors, hormonal therapy, clinical trials

PROFESSIONAL ACTIVITIES

CLINICAL

Fellow, Hematology/Oncology: During the clinical phase of my training from 2007-2009 I worked on the inpatient Hematology/Oncology consult services at UCSF, SFGH, and the VAMC as well as in the twice weekly at either the VAMC, SFGH, or Mt. Zion oncology clinics. During the research phase from 2009-2010 I worked twice weekly in the Mt Zion Genitourinary Oncology clinic.

Attending, Genitourinary Medical Oncology, UCSF: Since 2010 I have seen patients and served as an attending physician in the Mt Zion Genitourinary Medical Oncology clinic weekly, seeing patients and supervising rotating fellows, residents and medical students.

Attending, San Francisco General Hospital and SFGH Oncology Clinic: Since July 2011 I have been personally seeing patients in the SFGH general oncology clinic one day per week and have attended on the inpatient Oncology Consult service at San Francisco General Hospital 8 weeks out of the year, supervising fellows, residents and medical students.

SUMMARY OF CLINICAL ACTIVITIES

Attending, Genitourinary Medical Oncology, UCSF: Since 2010 I have seen patients and served as an attending physician in the Mt Zion Genitourinary Medical Oncology clinic weekly, seeing patients and supervising rotating fellows, residents and medical students.

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PROFESSIONAL ORGANIZATIONS

Memberships

2008 -	American Society of Clinical Oncology
2010 -	American Association of Cancer Researchers

Service to Professional Organizations

2012 -	American Society of Clinical Oncology, General Meeting	Prostate Cancer Poster Discussant

SERVICE TO PROFESSIONAL PUBLICATIONS

2011 -	Ad hoc referee for the following journals: Journal of Clinical Oncology, Cancer, Clinical Genitourinary Cancer, Urology, European Urology, Molecular Cancer Therapeutics, Growth Hormone and IGF Research, Human Mutation, and The Protein Journal

INVITED PRESENTATIONS

INTERNATIONAL

2012	Advances in Circulating Tumor Cell Conference Committee, Athens, Greece	Oral presentation

NATIONAL

2012	American Society of Clinical Oncology Genitourinary Symposium	Poster Presentation
2011	American Society of Clinical Oncology Genitourinary Symposium	Oral Plenary Abstract
2010	American Society of Clinical Oncology, Annual Meeting	Poster Presentation
2010	American Society of Clinical Oncology, Genitourinary Symposium	Poster Presentation

REGIONAL AND OTHER INVITED PRESENTATIONS

2013	UCSF Bladder Cancer Support Group	Oral Presentation
2013	UCSF Hematology Oncology Research Retreat	Poster Presentation
2012	UCSF Prostate Cancer Research Retreat	Oral Presentation
2012	UCSF Radiation Oncology Department Grand Rounds	Oral Presentation
2012	SFGH Cancer Awareness Resources and Education	Oral Presentation
2011	UCSF Hematology Oncology Research Retreat	Oral Presentation
2011	UCSF Hematology Oncology Research in Progress Seminar	Oral Presentation
2011	UCSF Bladder Cancer Research Retreat	Oral Presentations
2011	SFGH Cancer Awareness Resources and Education	Oral Presentation
2011	UCSF Prostate Cancer Research Retreat	Poster Presentation
2010	Pfizer Inc. Research Conference	Oral Presentation
2010	UCSF Urologic Oncology Seminar Series	Oral Presentation
2010	UCSF Hematology Oncology Research Retreat	Oral Presentation
2009	SFGH Cancer Awareness Resources and Education	Oral Presentation
2009	Stanford University 11th Annual Multidisciplinary Management of Cancer	Discussant
2009	Cancer and Lymphoma Group B (CALGB) Early Career Investigators Meeting	Oral Presentation

CONTINUING EDUCATION COURSES ATTENDED

2007	UCSF Hematology/Oncology weekly Clinical Case Conference
2007	UCSF Hematology/Oncology weekly Journal Club

UNIVERSITY AND PUBLIC SERVICE

UNIVERSITY SERVICE

SCHOOL OF MEDICINE

2009 - 2011	M3 Oncology	Small Group Leader

DEPARTMENTAL SERVICE

2010 - 2011	UCSF Division of Hematology Oncology	Chief Fellow

PUBLIC SERVICE

2009 - 2012	SFGH Cancer Awareness Resources Education (CARE)	Speaker

SUMMARY OF SERVICE ACTIVITIES

As Chief Fellow I organized and planned fellowship recruitment and orientation, designed fellows' schedules, implemented year-long performance-improvement projects, served as liaison to program director and division faculty, and mentored junior fellows.

Working with the CARE program at SFGH, giving talks 2-3 times per year I help discuss new trends in oncology management and strategies for survivorship in a Spanish-language community outreach and support program.

TEACHING AND MENTORING

TEACHING

FORMAL SCHEDULED CLASSES FOR UCSF STUDENTS

Qtr	Academic Yr	Course Number and Title	Teaching Contribution	Units	Class Size
F	2009 - 2011	M3: Mechanisms, Molecules, and Malignancies	Discussion Group Leader; 2 two hour sessions		12

POSTGRADUATE AND OTHER COURSES

2011 - 2012	Hematology Oncology Fellowship Didactic Lectures	Introduction to Bladder cancer
2011 - 2012	Internal Medicine Residency Noon Lectures	Updates in Prostate Cancer

INFORMAL TEACHING

2010 - 2012 Genitourinary Clinic Attending (weekly with fellow, resident, or medical student)

2011 - 2012 SFGH Oncology Consult Service (8 weeks, with fellows, residents, and/or medical students)

TEACHING NARRATIVE

My teaching activities consist of a combination of formal sessions with medical students as a discussion group leader, didactic sessions with the first year oncology fellows and with residents, and informal teaching with fellows, residents, and students in the oncology clinics and on the wards.

MENTORING

TEACHING AND MENTORING AIDS

Prostate Cancer Treatment and Research Handout for patients in GU Medical Oncology clinic, describing how prostate cancer is treated and describing current UCSF research

SUMMARY OF TEACHING AND MENTORING HOURS

2010 - 2011	130 total hours of teaching (including preparation)
	Formal class or course teaching hours: 20 hours
	Informal class or course teaching hours: 110 hours
	Mentoring hours: 0 hours
	Other hours:
2011 - 2012	240 total hours of teaching (including preparation)
	Formal class or course teaching hours: 20 hours
	Informal class or course teaching hours: 220 hours
	Mentoring hours: 0 hours
	Other hours:
2012 - 2013	240 total hours of teaching (including preparation)
	Formal class or course teaching hours: 20 hours
	Informal class or course teaching hours: 220 hours

Mentoring hours: 0 hours

Other hours:

2013 - 2014 Total anticipated hours of teaching: 240 hours

RESEARCH AND CREATIVE ACTIVITIES

RESEARCH AWARDS

CURRENT

A119352 (PI) 03/01/2012 - 02/28/2015

Prostate Cancer Foundation

Investigation of Genomic Mechanisms of Androgen Biosynthesis Inhibitor Resistance in Castration Resistant Prostate Cancer

P0043122 (PI) 05/01/2012 - 04/30/2017

Department of Defense

Investigation of Genomic Mechanisms of Androgen Biosynthesis Inhibitor Resistance in Castration Resistant Prostate Cancer

PAST

A114463 (PI) 07/01/2010 - 06/30/2011

American Society of Clinical Oncology, Young Investigator Award

Determination of Genotypic Markers of Docetaxel Resistance in Castration Resistant Prostate Cancer.

PEER REVIEWED PUBLICATIONS

1.

Friedlander TW, Roy R, Tomlins SA, Ngo VT, Kobayashi Y, Azameera A, Rubin MA, Pienta KJ, Chinnaiyan A, Ittmann MM, Ryan, CJ, Paris PL, “Common Structural and Epigenetic and Changes in the Genome of Castration Resistant Prostate Cancer” Cancer Res. 2012 Feb 1;72(3):616-25.

2. Friedlander TW, Ryan CJ. "Targeting the Androgen Receptor" Urol Clin N Am 2012 Nov (39): 453-464

3.

Friedlander TW, Weinberg VK, Huang Y, Mi JT, Formaker CG, Small EJ, Harzstark AL, Lin AM, Fong L, Ryan CJ. “A Phase II Study of Insulin-like Growth Factor Receptor Inhibition with

Nordihydroguaiaretic Acid in Men with Non-Metastatic Hormone Sensitive Prostate Cancer". Oncol. Rep. 2012 Jan;27(1):3-9.

4.

Friedlander TW, Ryan CJ. Editorial Comment on "Adrenocorticotropic hormone (ACTH) regulates androgen synthesis in men receiving androgen deprivation therapy for localized prostate cancer". J Urol. 2010 Nov;184(5):1976.

5.

Friedlander TW, Weinberg VK, Small EJ, Sharib J, Harzstark AL, Lin AM, Fong L, Ryan CJ. Effect of the Somatostatin Analog Octreotide Acetate on Circulating Insulin-Like Growth Factor-1 and Related Peptides in Patients with Castration-Resistant Prostate Cancer (CRPC): Results of a Phase II Study. Urol Oncol. 2010: Sep 28. Epub ahead of print.

Review Articles

1.

Friedlander TW, Ryan CJ. Novel hormonal approaches in prostate cancer. Curr Oncol Rep 2009;11:227- 234.

Books and Chapters

1.

Friedlander, T.W. Ryan, C.J. (2010). "Andrenal Androgen Synthesis Inhibitor Therapies in Castration Resistant Prostate Cancer." In W. Figg, E. Small, C. Chau (Eds.), *Drug Management of Prostate Cancer*. (pp 91-100). Totowa: Humana Press.

Other Publications

1.

Friedlander, TW; Ryan CJ. "Beyond the Abstract – Functional phenotyping and genotyping of circulating tumor cells from patients with castration resistant prostate cancer." UroToday 7 Aug. 2009. Available from: http://www.urotoday.com/3341/browse_categories/beyond_the_abstract/beyond_the_abstract__function al_phenotyping_and_genotyping_of_circulating_tumor_cells_from_patients_with_castration_resistant_pros tate_cancer08072009.html

ABSTRACTS

1.

Terence W. Friedlander, Vivian K. Weinberg, Alex Yeung, James Burke, Donald L. Lamm, James M. McKiernan, John J. Nemunaitis, Joe Stephenson Jr., Eric Jay Small, Lawrence Fong, Maxwell V. Meng; **Activity of intravesical CG0070 in rb-inactive superficial bladder cancer after BCG failure: Updated results of a phase I/II trial.**

Presented at ASCO Genitourinary Symposium and ASCO Annual Meeting 2012

RESEARCH PROGRAM

My research is focused on understanding the biology of advanced prostate and bladder cancers and developing novel therapeutics to treat these diseases. Specifically I am interested in understanding the genomics of advanced prostate cancer through the acquisition of castration-resistant biopsies and circulating tumor cells, then using array based techniques to identify pathways and mechanisms of treatment resistance.

SIGNIFICANT PUBLICATIONS

See "Peer Reviewed Publications" above

ADDITIONAL RELEVANT INFORMATION:

Fluent in Spanish, conversant in French and Italian